The Transfusion System in Germany

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German Transfusion System Between AIDS shock and European Blood Directive

- Blood components considered as drugs (Drug act 1976):
  - Manufacturing license for blood establishments by regional authorities
  - GMP inspections by regional authorities
  - Individual marketing authorization for blood components by Paul-Ehrlich-Institut (PEI) as competent federal authority
  - Competence to impose mandatory requirements by PEI
  - Pharmacovigilance by PEI: collection and assessment of spontaneous notifications of suspected severe adverse drug reactions, line listing of non-severe adverse drug reactions

- IVD considered as drugs
  - Individual marketing authorization for IVD by PEI as competent authority
  - Batch release by PEI
Between AIDS shock and European Blood Directive

- Transfusion Act 1998, regulating basic requirements for
  - Donor information, protection, selection, and testing
  - Documentation of blood donation
  - Documentation of Use
  - Look back procedure
  - Notification of suspicion of severe and non-severe adverse reactions by blood establishments and physicians to PEI
  - Notification of the quantity of donation, manufacturing and use of blood products by blood establishments and physicians to PEI
  - Notification of donor epidemiology (HIV, HBV, HCV, Lues) by blood establishments to Robert Koch-Institute (RKI)
  - German Medical Association (BÄK), in liaison with the PEI, responsible for “Guidelines on the Collection of Blood and Blood Components and on the Use of Blood Products (Hemotherapy)”
Transfusion Chain

Manufacturer
(Drug Law)

Transport
Storage (Blood bank, ward)

Transport in Hospital
(Transfusion Law)

Collection
Release

Transport

Information
Transfusion
Documentation

Screening
Manufacture
Testing

Donor Selection

Diagnosis, Treatment
Cooperating parties for blood safety

Robert Koch-Institut
- Epidemiology

Blood Establishments

German Medical Association
- Guidelines

31 Regional Authorities
- Manufacturing Licenses
  - GMP inspections

Paul-Ehrlich-Institut
- Marketing Authorization
  - (blood components, IVD)
  - Pharmacovigilance
  - IVD-Vigilance

Hospitals

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National Advisory Committee Blood „AK BLUT“

Members installed by the Ministry of Health represent

- scientific societies,
- different organizational structures of blood establishments,
- medical disciplines involved in blood transfusion and treatment of hemophilia
- Industry (Plasma Derivatives, IVD)
- Patient groups
- Federal authorities
- PEI

Main Tasks are

- Discussion of actual opportunities and emerging threats
- Preparing votes and opinions as a result of these discussions
- Expert advice for Federal and Regional Authorities
Research and Education as Main Pillars of Transfusion Safety

- Red cross and university blood establishments
  - Education of physicians, responsible for transfusion in hospitals
  - Research on hemostasis, immunohemotherapy, blood component quality, stem cell therapy, hereditary coagulation disorders, blood component safety, donor epidemiology

- Paul-Ehrlich-Institute
  - Research on hemostasis, blood component quality and safety, donor epidemiology, hemovigilance - often done in cooperation with blood establishments

- Robert Koch-Institute
  - Research on donor epidemiology

- Co-operation of scientists under the head of AK Blut
  - Relevance of different blood-borne pathogens for blood product safety, standardized review publications on: CJD, vCJD, HIV, HBV, HCV, HAV, HCMV, HEV, HTLV, GBVC, Treponema, Yersinia, Parvovirus B19, TTV, Coxiella burnetii, influenza, arbobacteria, arboviruses
German Transfusion System and European Legislation regulating blood components

- **93/42/EC** Medical Devices – standards for blood bags systems
- **98/79/EC** In-Vitro-Diagnostics – standards for screening tests - Licensing and batch release by PEI ceased - Loss of control
- **2002/98/EC** Standards of quality and safety for collection, testing, processing, storage, distribution of blood components – hemovigilance
- **2004/33/EC** Technical requirements for blood components
- **2005/61/EC** Look-back and Hemovigilance – *requirement of annual notification to the commission of*
  - serious adverse events which may influence product quality and safety
  - serious adverse reactions which may be due to product quality and safety
- **2005/62/EC** Quality system
Different Organizational Structures of Blood establishments in Germany (2007)

- Red Cross: 9
- Plasma Industry: 18
- Private: 1
- Army: 1
- Other (Communal, University, Foundation establishments): 22

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RBC Processing from Whole Blood Donation and Apheresis by blood establishments of different structures

Transfusion Units x 10^6

- Red Cross
- Others
- Private
- Army

Plasma for fractionation (Whole blood donation and apheresis): Collection by blood establishments of different structures

- Red Cross
- Others
- Plasma Industry
- Private

<table>
<thead>
<tr>
<th>Year</th>
<th>Red Cross</th>
<th>Others</th>
<th>Plasma Industry</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td></td>
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<td>2006</td>
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</table>
Average Blood Supply

- **2005-2006 average for Germany**
  - 57 Whole Blood donations per 1000 inhabitants
  - 53 RBC provided per 1000 inhabitants

- **2004 average for European Countries**
  - 37 Whole Blood donations per 1000 inhabitants
  - 37 RBC provided per 1000 inhabitants
Practical Experience:
Percentage of refused Requests for RBC (Red Cross West 2006)

Answer: Optimal Use?
## Blood Safety

### Average annual number of blood components distributed in Germany from 2000 to 2006

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
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<tbody>
<tr>
<td>RBC</td>
<td>4,412,900</td>
</tr>
<tr>
<td>PC</td>
<td>404,400</td>
</tr>
<tr>
<td>FFP</td>
<td>1,227,200</td>
</tr>
<tr>
<td><strong>Total/year</strong></td>
<td><strong>6,044,500</strong></td>
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</tbody>
</table>

### Transfusion transmitted viral infections from 1994 to 2007, assessed as probable

<table>
<thead>
<tr>
<th>Infection</th>
<th>Number</th>
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<tbody>
<tr>
<td>HIV</td>
<td>7</td>
</tr>
<tr>
<td>HBV</td>
<td>53</td>
</tr>
<tr>
<td>HCV</td>
<td>34</td>
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<tr>
<td><strong>Total/14 years</strong></td>
<td><strong>84</strong></td>
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</tbody>
</table>

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Transfusion transmitted bacterial infections, assessed as probable

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</thead>
<tbody>
<tr>
<td>RBC: 26</td>
<td>4 (2)</td>
<td>5 (2)</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>PC: 32</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>2 (1)</td>
<td>4</td>
<td>3 (1)</td>
<td>4 (1)</td>
<td>3 (1)</td>
<td>6 (1)</td>
<td>4</td>
</tr>
<tr>
<td>FFP: 5</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Sum: 63</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>2</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>9</td>
<td>6</td>
</tr>
</tbody>
</table>

All but one (day 4) of fatal PC transmissions were transfused on day 5 of storage.

9 deaths caused by 6 PC, and 4 RBC, i.e., one patient died on average per year and per 400,000 PC administered.
Pathogen reduced Blood Components despite an extremely low risk of transfusion transmitted pathogens?

- Pathogen inactivation of blood components is not required as a nation wide measure with respect to risk of HIV, HCV, HBV transmission.
- However, establishments can apply for a marketing authorization of pathogen inactivated blood components.
- Possible gain in platelet safety despite infectivity against spores?
- Adding to the already high safety achieved by pathogen screening (e.g. in case of errors or test failures)
- Preparedness in case of new emerging diseases / pandemic without test available
Ultimate Goal

🌈 Supply of blood products to meet the needs of patients
  - in sufficient amount,
  - with good quality,
  - with reliable efficacy,
  - with an acceptable safety.

🌈 To achieve this object is in the responsibility of
  - manufacturers,
  - official regulatory bodies.